REMARKS

Claims 24-33, 35-39 and 41-49 are pending and subject to examination. Claims 35 and 36 are currently amended.

Formal Drawings

Corrected drawings were required. These are submitted herewith.

Objection to Claim 35

Claim 35 has been amended and now depends from claim 26.

Claim Rejections under § 112, 2nd

Claim 26 has been amended to correct the syntactical error.

Claim rejections under § 103

Claims 24-33, 35-39 and 41-49 are newly rejected as obvious over Hsu (US 5,958,891), Janeway, Pouwels and Medaglini. The Applicants respectfully traverse the rejection since there is no motivation to combine the references nor a reasonable expectation of success.

1. There is no motivation to combine the references.

Janeway teaches that there are two factors that figure significantly in determining whether IgE is produced. These two factors are (i) the route of antigen presentation and (i) the nature of the antigen. Janeway presents this in the first paragraph of Section 12-1:

> There are certain **antigens** and **routes of antigen presentation** to the immune system that **favor the production of IgE**. . . . Antigens that selectively evoke Th2 cells that drive an IgE response are known as allergens. [Section 12-1, ¶ 1]

a. Nature of the antigen.

In the above-quoted passage, Janeway stresses that when an antigen is an allergen it drives IgE production. Since the claimed methods use bacteria that express allergens, at least as far as the nature of the antigen is concerned, Janeway teaches that the methods would be expected to increase ("drive") IgE production.

b. Route of presentation.

Now turning to the route of presentation, above the paragraph quoted above, immediately adjacent to the section number 12-1, Janeway states in bold:

> **Allergens are often delivered transmucosally at low dose, a route that favors IgE production.**

The claimed methods use oral administration, and, thus, transmucosal delivery. As seen above, in addition to teaching that allergens increase IgE production, Janeway teaches that transmucosal delivery also increases IgE production. The Applicants respectfully submit that **Janeway teaches away from the claimed method**. Put differently, one reading Janeway would not choose to deliver an allergen transmucosally to **suppress** IgE production when Janeway asserts that the combination "**favors** IgE production."

The remainder of Janeway is not to the contrary. The Examiner notes that Th2 cells can switch antibody isotype by quoting the paragraph, reproduced in full below:

> There are certain **antigens** and **routes of antigen presentation** to the immune system that **favor the production of IgE**. As we learned in Chapter 9, T_H2 cells can switch the antibody isotype from IgM to IgE, or they can cause switching to IgG2 and IgG4 (human) or IgG1 and IgG3 (mouse). Antigens that selectively evoke T_H2 cells that **drive an IgE response** are known as allergens. [Section 12-1, ¶ 1]

But read properly, Janeway teaches that the administration of an allergen causes switching to IgE, not to IgG. Thus, one skilled in the art would not use an allergen to reduce IgE production, since allergens would evoke T_H2 cells to switch to the IgE isotype.

Instead, one might use peptides, rather than allergens, as suggested under section 12-15 of Janeway:

> An alternative and still experimental approach to desensitization is vaccination with **peptides derived from common allergens**. This procedure induces T-Cell anergy in vivo associated with multiple changes in the T-cell phenotype, including downregulation of cytokine production and of expression of the T-cell receptor:CD3 complex. IgE-mediated responses are not induced because **IgE can recognize only the intact antigen**.

Peptides derived from allergens differ from allergens themselves. For example, Janeway explains above that IgE can recognize intact allergens, but not peptides. The methods described in the present claims do not use peptides.

The other desensitization method taught by Janeway uses injections. Injections do not use a transmucosal route of delivery, in contrast to the oral administration of a bacterium. Although Applicants take no position as to whether Janeway's suggested desensitization methods are enabled or deserve any weight, Janeway suggests desensitization methods that differ from the claimed methods with respect to (i) nature of the antigen and (ii) route of delivery, the two very factors that Janeway taught were significant.

MPEP § 2141.03 provides direction for evaluating references with respect to obviousness. This section states in a subheading, "prior art must be considered in its entirety, including disclosures that teach away from the claims." Janeway must be considered in its entirety. To summarize, Janeway teaches that the transmucosal delivery of allergens results in increased IgE production. Methods for desensitizing either involve use of peptides, rather than allergens, and a route of delivery that is not transmucosal. **Thus, Janeway teaches away from the claimed methods and suggests desensitizing methods that differ from the claimed methods with respect to the two significant factors.**

In view of Janeway's textbook teachings and the fact that nothing in the other cited references diminishes Janeway's authority, one skilled in the art, seeking to **suppress** IgE production, would not combine the cited references to arrive at a method that Janeway specifically states "**favors** IgE production."[1]

[1] The Applicants do not concede that the combination of the cited references resembles the claimed methods.

2. There is no reasonable expectation of success for the alleged combination.

The Applicants respectfully submit the Examiner has not shown a **reasonable** expectation of success. Janeway asserts that "allergens are often delivered transmucosally at low dose, a route that **favors** IgE production." This assertion is evidence that there is no expectation of success for a decrease in IgE production by delivering an allergen transmucosally. **A result in direct contradiction to Janeway cannot be reasonably expected.**

The Applicants respectfully submit that all claims are in condition for allowance, which action is expeditiously requested. The Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor does the Applicants concede that there are not other good reasons for patentability of the presented claims or other claims. For example, the Applicants reserve the right to argue the Examiner's comments on Dr. Hsu's Declaration and characterization of the references.

Enclosed is a $475 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket number 12774-002001.

Respectfully submitted,

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